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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/673,288	12/07/00	CHEVALET L	PF83PCTSEQ/D

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HM12/0523

EXAMINER	
KATCHERES,K	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/673,288	Applicant(s) CHEVALET ET AL.	
	Examiner Konstantina Katcheves	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☒ Other: *notice to comply / detailed action* .

DETAILED ACTION

Claims 1-21 are pending in the instant action.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. The instant Application contains sequences on pages 8, 15, 17-19, 20 and 25, however fails to provide sequence identifiers (SEQ ID NO:). Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

For the purposes of compact prosecution, Applicant is given THREE MONTHS from the mailing date of this communication within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be

obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Abstract

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Warne et al. (Gene Vol.46 No.1 1986) (hereinafter "Warne") in view of Yanofsky et al. (Biochimie Vol.78 1996) (hereinafter "Yanofsky").

The invention of the instant claims is drawn to a method of expressing a protein of interest under the control of Ptrp promoter by transforming a cell with a vector encoding a nucleic acid sequence capable of inactivating TnaA tryptophanase. The invention is further drawn to the above constructs.

Warne teaches a plasmid vector construct wherein Ptrp promoter is operably linked to the trpR gene. The method of Warne improves the expression of a protein of interest before induction. Warne fails to teach a method of inactivating Tna tryptophanase as a method of repressing a protein of interest prior to induction.

Yanofsky teaches transciption antitermination mechanisms that regulate expression of the TnaA operon. The transcription termination protein Rho factor prevents the transcription and thereby the expression of Tna Tryptophanase.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the reference of Warne and Yanofsky to arrive at a method of expressing of expressing a protein of interest under the control of Ptrp promoter by transforming a cell with a vector encoding a nucleic acid sequence capable of inactivating TnaA tryptophanase and the vector required. One of ordinary skill in the art would have been motivated to resolve strict repression of the overproduction system before induction which is important when using an expression vector with high copy number since inactivation of TnaA tryptophanase would result in increased production of the protein of interest. Therefor, absent evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claim Rejections - 35 USC § 112

35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 12-14 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-9 are drawn to various nucleic acid sequences. Claims 12-14 are drawn vectors comprising "mutated fragments" of the TnaA tryptophanase coding sequence. Claim 17 is drawn to a vector comprising "biologically active fragments" of the TrpR tryptophan operon repressor.

Claims 12-14 and 17 are not adequately described in the disclosure of the instant invention. The specification teaches TnaA tryptophanase and the TrpR tryptophan operon repressor. However, the specification fails to disclose to one of skill in the art how to obtain the fragments embraced by the scope of the claims, how to screen for fragments, how to obtain fragments that are active, nor how to determine which nucleic acid sequences are embraced by the claims. Although the genes are disclosed in the specification, no description is provided that would allow the skilled artisan to readily envision what additions, mutations or deletions intended by Applicant in the practice of the invention. Furthermore, the specification fails to define what nucleic acids comprise those of claims 1-9 since the claims read on any nucleic

acids. The breadth of the claims encompass sequences that encode inactive TnaA tryptophanase or TrpR tryptophan operon repressor. Moreover, since the specification does not teach what amino acid residues are required for the claimed activity of the above proteins, the skilled artisan would not recognize that Applicants were in possession of any and all proteins or fragments thereof embraced by the claims.

35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 16 recite the limitation that "all or part of the sequence of a promoter." The language "all or part" renders the instant claim vague and indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

Claim 1 refers to a "nucleic acid sequences" several times in the method steps. However, it is unclear whether Applicant is referring back to the gene encoding a protein of interest or some other sequence altogether.

Claim 1 also recites a gene encoding a protein of interest. The preamble of the claim recites that a gene of interest is place under the control of the Ptrp promoter which implies they are in the same construct. Step (b) recites transforming a cell with a vector "containing" a gene

encoding a protein of interest. Due to internal inconsistencies of the steps of the method, it is unclear whether the gene is in the same vector of the Ptrp promoter.

Claim 2 is rejected as being incomplete. Claim 2 refers to methods described in "Example 1 or 2" as a limitation to the method of the claims. Although claims are read in light of the specification, a claim should be complete within itself whenever possible. Therefor, claim 2 should incorporate the intended steps in the examples recited in the claim to obviate the instant rejection.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. Claim 5 recites limitations to the method of claim 1 wherein a resolution step and a screening step are between steps (a) and (b) of claim 1. The instant claims fails to indicate how the resolution and screening steps are to be accomplished, thus rendering the claims vague and indefinite.

Claim 6 recites the language "by any means." This language provides no guidance as to the breadth of the claim and by the very nature of the words "any means" renders the metes and bounds of the claim impossible to determine.

Claims 10-17 are drawn to a construct. The claims are improper because the "first construct" claimed must be preceded by an article.

Claim 10 recites the limitation "the Ptrp operon promoter." There is insufficient antecedent basis for this limitation in the claim. The rejection would be obviated if "a Ptrp operon promoter" were recited.

Claim 12 recites the limitation "the Ptna tryptophanase operon promoter." There is insufficient antecedent basis for this limitation in the claim. The rejection would be obviated if "a Ptna tryptophanase operon promoter" where recited instead.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Konstantina Katcheves whose telephone number is (703) 305-1999. The examiner can normally be reached on Monday through Friday 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Konstantina Katcheves
May 17, 2001

ANDREW WANG
PATENT EXAMINER
TC1600

Notice to Comply	Application No.	Applicant(s)	
	09/673288	Chevalet et al.	
	Examiner	Art Unit	
	Konstantina Katcheves	1636	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
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